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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,896	10/16/2006	Ferdinand Hermann Bahlmann	P/2107-297	4965
2352 7590 08/06/2009 OSTROLENK FABER GERB & SOFFEN 1180 AVENUE OF THE AMERICAS NEW YORK, NY 100368403			EXAMINER DEBERRY, REGINA M	
			ART UNIT 1647	PAPER NUMBER
			MAIL DATE 08/06/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/586,896	Applicant(s) BAHLMANN ET AL.	
	Examiner Regina M. DeBerry	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-6, 10, 15, 19, 32, 39, 40, 45, 49 and 52-64 is/are pending in the application.
- 4a) Of the above claim(s) 4-6, 10, 15, 19, 32, 39, 40, 45, 49, 52, 53 and 58-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 54-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 4-6, 10, 15, 19, 32, 39, 40, 45, 49 and 52-64 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/20/06, 5/18/07, 6/2/08, 5/27/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment, filed 20 July 2006, has been entered in full. Claims 7, 8, 11-14, 16-18, 20-31, 33-38, 41-44, 47, 48 and 51 are canceled. The amendment, filed 29 April 2009, has been entered in full. Claims 40 and 53 are amended. Claims 1-3, 9, 46, and 50 are canceled. New claims 54-64 were added.

Applicant's election without traverse of Group I (claims 1-3, 9, 40, 46, 50 and 53) in the reply filed on 29 April 2009 is acknowledged.

Matter of Record

The Examiner stated in the previous Election/Restriction (31 March 2009) that the instant application employed improper "use claims" and that it was unclear if Applicant is intended to claim a composition or a method/process. The Examiner attempted to separate between claims drawn to compositions and claims drawn to methods. The Examiner stated that the Election/Restriction would be adjusted once the claims were amended to proper form.

In response to the Election requirement, Applicant states that in light of the improper "use" claims in Group I, the claims have been rewritten as new claims 54-57. Applicant states that the election should be deemed as constituting an election of Group I, claims 40, 53 and new claims 54-64. Applicant states that should the Examiner

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choose to make a further restriction after considering the new and amended claims, Applicant provisionally elects claims 54-57.

Applicant's arguments have been fully considered and are deemed partly persuasive. Claims 40, 53, 54-64 are drawn to both products and different methods. However, the Examiner accepts Applicant's election of claims 54-57. Claims 4-6, 10, 15, 19, 32, 39, 40, 45, 49, 52, 53, 58-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 29 April 2009.

Information Disclosure Statement

The information disclosure statement(s) (IDS) (filed 7/20/06, 5/18/07, 6/2/08, and 5/27/09) were received and comply with the provisions of 37 CFR §§1.97 and 1.98. They have been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 54-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are drawn to a method for treating a human or animal exhibiting at least one dysfunction of endothelial progenitor cells, at least one cardiovascular risk and at least one end-organ damage comprising administering EPO or a derivative thereof. The claims are indefinite because it is not clear what is actually being treated and/or what is being exhibited in the human/animal. For example, are the claims drawn to treating at least one dysfunction of endothelial progenitor cells, wherein the human/animal exhibits at least one end-organ damage and at least one cardiovascular risk? Are the claims drawn to treating at least one end-organ damage, wherein the human/animal exhibits at least one dysfunction of endothelial progenitor cells and at least one cardiovascular risk? Are the claims drawn to treating any disease, wherein the human/animal exhibits at least dysfunction of endothelial progenitor cells, at least one cardiovascular risk and at least one end-organ damage?

Lastly, the claims should recite the goal that must be achieved. The claims do not have a step that clearly relates back to the preamble (i.e. “..wherein ____ is treated in said human or animal patient”).

The metes and bounds of the instant claims cannot be determined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The specification as originally filed does not provide support for the invention as now claimed: new claims 54-57.

Applicant's amendment, filed 29 April 2009, asserts that no new matter has been added and directs support to claims 1-3, 9, 46 and 50. However, the wording or connotation of the instant claims is not readily apparent from said section. Applicant does not provide direction for the written description for the above-mentioned "limitations" in the body of the specification and the Examiner cannot locate the wording or connotation of the instant claims (i.e. diseases or conditions which have at least one dysfunction of endothelial progenitor cells AND at least one cardiovascular risk AND at least one end-organ damage).

The specification as filed does not provide a written description or set forth the metes and bounds of these "limitations". The instant claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to provide *specific written support* for the

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“limitations” indicated above or rely upon the limitations set forth in the specification as filed.

Claims 54-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant Examples teach the effects of administered EPO in subjects with renal anemia and chronic renal failure. Example 1 teaches increased mobilization and an increase in the number of endothelial progenitors cells in patients with renal anemia (as a consequence of renal disease in pre-terminal renal failure stage). Patients were treated with 5000 IU of rhEPO. (pages 79-81). The specification teaches the limitation “dysfunction” to include impairment of proliferation, differentiation or motility (page 34). Examples 3 and 4 teach the reduction in the progression of chronic and acute renal failure upon administering EPO in rat animal models (pages 82-84).

The claims are not enabled for the following reasons.

1. The instant claims encompass treating **any disease** in a subject who exhibits at least one dysfunction of endothelial progenitor cells, at least one cardiovascular risk and at least one end-organ damage comprising administering EPO or a derivative thereof. The instant claim encompasses treating diverse diseases such AIDS, various cancers, an assortment of heart conditions, etc. Many different diseases can result in

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secondary conditions which present as dysfunction of endothelial progenitor cells, cardiovascular risk and end-organ damage. The instant examples only employ a renal disease patient population.

2. The specification fails to teach wherein a patient exhibits **at least one cardiovascular risk *in addition*** to one dysfunction of endothelial progenitor cells and at least one end-organ damage. The Examples teach that EPO treats at least one dysfunction of endothelial cells (such as increasing endothelial proliferation) and reduces the progression of chronic and acute renal failure upon administering EPO in rat animal models. While one skilled in the art could assume that renal failure would also encompass at least one dysfunction of endothelial progenitor cells. The specification fails to teach that the same patient population also exhibits at least one cardiovascular risk.

Lastly, the claims encompass derivatives of EPO. The specification teaches derivatives as encompassing EPO structures wherein one or more residues are substituted. The specification also states that derivatives include fusion proteins, in which functional domains of another protein are present on the N-terminal part or on the C-terminal part (pages 22-23). The specification does not teach how to make any derivative of the exemplified EPO polypeptide. The specification would not support claims to EPO polypeptides modified to an unlimited extent relative to those exemplified. In order to make a sequence derivative, for example, with the reasonable assurance that it would have the desirable properties of the invention, the artisan would need to know which regions of the disclosed polypeptide (i.e. EPO and the other

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proteins functional domains) are responsible for the interactions underlying its biological function(s). As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. The specification fails to teach the functional domains of other proteins that can be employed as a fusion protein with EPO. The specification states that GM-CSF, VEGF, a statin or another factor may be employed (page 23). However, these are prophetic teachings. The disclosure provides no guidance as to which regions of the proteins would be tolerant of modification and which would not, and it provides no working example of any variant sequence which would be within the claims. The instant Examples employ EPO, not derivatives thereof. It is in no way predictable that randomly selected mutations, deletions, *etc.* in the disclosed EPO sequence would afford a protein having activity comparable to the one disclosed. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions. Please see Wells, J.A. (Additivity of Mutational Effects in Proteins. *Biochemistry* 29:8509-8517; 1990) and Ngo et al. (Computational Complexity, Protein Structure Prediction and the Levinthal Paradox. *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 433-440 and 492-495; 1994). The artisan would accordingly have no resort save trial-and-error experimentation to determine which of the astronomically large number of possible

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structural variants had the functional properties of the claimed proteins. For the reasons discussed above, such experimentation would be undue for one skilled in this art.

Due to the large quantity of experimentation necessary to treat any disease in a patient who exhibits at least one dysfunction of endothelial progenitor cells, at least one cardiovascular risk and at least one end-organ damage comprising administering EPO or a derivative thereof, the large quantity of experimentation necessary to generate the infinite number of EPO derivatives recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in EPO derivatives in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural limitations for EPO derivatives and limitations regarding diseases which encompass dysfunction of endothelial progenitor cells, cardiovascular risk and end-organ damage that can be treated with EPO, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647

/R. M. D./
Examiner, Art Unit 1647
8/1/09